ATP1A2 gene

ATPase Na+/K+ transporting subunit alpha 2

Normal Function

The *ATP1A2* gene provides instructions for making one part (the alpha-2 subunit) of a protein known as a Na+/K+ ATPase. This protein uses energy from a molecule called adenosine triphosphate (ATP) to transport charged atoms (ions) into and out of cells. Specifically, it pumps sodium ions (Na+) out of cells and potassium ions (K+) into cells.

Na+/K+ ATPases that include the alpha-2 subunit are primarily found in nervous system cells called glia, which protect and maintain nerve cells (neurons). Through its action in glia, the protein plays a critical role in the normal function of neurons. Communication between neurons depends on chemicals called neurotransmitters. To relay signals, a neuron releases neurotransmitters, which attach to receptor proteins on neighboring neurons. After the neurotransmitters have had their effect, they detach from their receptors and are removed from the spaces between neurons by glia. This process is carefully regulated to ensure that signals are transmitted accurately throughout the nervous system. The Na+/K+ ATPase helps regulate this process by stimulating glia to clear neurotransmitters from the spaces between neurons. This protein also removes excess potassium ions from these spaces.

Health Conditions Related to Genetic Changes

alternating hemiplegia of childhood

At least one mutation in the *ATP1A2* gene can cause alternating hemiplegia of childhood. The primary feature of this condition is recurrent episodes of temporary paralysis, often affecting one side of the body (hemiplegia). During some episodes, the paralysis alternates from one side to the other or affects both sides of the body at the same time. The known *ATP1A2* gene mutation associated with this condition replaces a single protein building block (amino acid) in Na+/K+ ATPase: the amino acid threonine is replaced with the amino acid asparagine at protein position 378 (written as Thr378Asn or T378N). This genetic change probably impairs the protein's ability to transport ions, although it is unclear how the mutation leads to the specific features of alternating hemiplegia of childhood.

familial hemiplegic migraine

More than 30 mutations in the *ATP1A2* gene have been identified in people with familial hemiplegic migraine type 2 (FHM2). This condition is characterized by migraine headaches with a pattern of neurological symptoms known as aura. In

FHM2, the aura includes temporary numbness or weakness on one side of the body (hemiparesis). Most of the mutations involved in FHM2 change single amino acids in the Na+/K+ ATPase protein. Some mutations impair the protein's ability to transport ions. Others prevent the production of any protein from one copy of the *ATP1A2* gene in each cell. As a result, less potassium is pumped into neurons, less sodium is pumped out of these cells, and neurotransmitters spend more time in the spaces between neurons. The resulting changes in signaling in the brain lead people with FHM2 to develop these severe headaches.

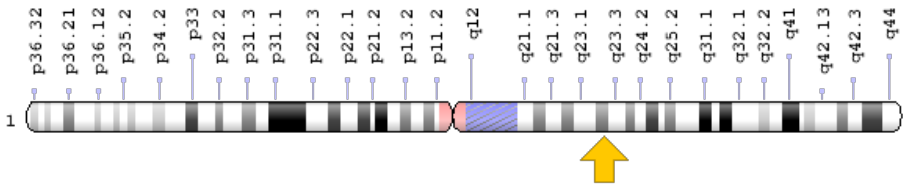
sporadic hemiplegic migraine

ATP1A2 gene mutations can also cause sporadic hemiplegic migraine. The signs and symptoms of this condition are identical to those of FHM2 (described above); however, sporadic hemiplegic migraine occurs in people with no family history of the condition. As in FHM2, most of the mutations associated with sporadic hemiplegic migraine change single amino acids in the Na+/K+ ATPase protein. These changes impair the function of the protein. Although the mutations that cause sporadic hemiplegic migraine are not as well-studied as those in familial hemiplegic migraine, it is thought that they have similar effects: impairing the transport of sodium and potassium ions and prolonging the presence of neurotransmitters between neurons. The abnormal signaling resulting from these changes leads to the headaches and auras characteristic of the condition.

Chromosomal Location

Cytogenetic Location: 1q23.2, which is the long (q) arm of chromosome 1 at position 23.2

Molecular Location: base pairs 160,115,730 to 160,143,591 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AT1A2_HUMAN
- ATPase, Na+/K+ transporting, alpha 2 (+) polypeptide

- ATPase, Na+/K+ transporting, alpha 2 polypeptide
- FHM2
- MHP2
- Na+/K+ ATPase 2
- Na+/K+ -ATPase alpha 2 subunit proprotein
- Na+/K+ ATPase, alpha-A(+) catalytic polypeptide
- Na+/K+ ATPase, alpha-B polypeptide
- sodium-potassium ATPase
- sodium pump 2
- sodium pump subunit alpha-2
- sodium/potassium-transporting ATPase alpha-2 chain

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1998): The ATP-Dependent Na+,K+ Pump
  https://www.ncbi.nlm.nih.gov/books/NBK28174/

GeneReviews

- Familial Hemiplegic Migraine
  https://www.ncbi.nlm.nih.gov/books/NBK1388

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ATP1A2%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ATPase, Na+/K+ TRANSPORTING, ALPHA-2 POLYPEPTIDE
  http://omim.org/entry/182340

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ATP1A2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ATP1A2%5Bgene%5D

- HGNC Gene Family: ATPase Na+/K+ transporting subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/1208
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=800
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/477
- UniProt
  http://www.uniprot.org/uniprot/P50993

Sources for This Summary

- Bassi MT, Bresolin N, Tonelli A, Nazos K, Crippa F, Baschirotto C, Zucca C, Bersano A, Dolcetta D, Boneschi FM, Barone V, Casari G. A novel mutation in the ATP1A2 gene causes alternating hemiplegia of childhood. J Med Genet. 2004 Aug;41(8):621-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15286158
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735877/
- Castro MJ, Nunes B, de Vries B, Lemos C, Vanmolkot KR, van den Heuvel JJ, Temudo T, Barros J, Sequeiros J, Frants RR, Koenderink JB, Pereira-Monteiro JM, van den Maagdenberg AM. Two novel functional mutations in the Na+,K+-ATPase alpha2-subunit ATP1A2 gene in patients with familial hemiplegic migraine and associated neurological phenotypes. Clin Genet. 2008 Jan;73(1):37-43. Epub 2007 Nov 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18028456
- Jurkat-Rott K, Freilinger T, Dreier JP, Herzog J, Göbel H, Petzold GC, Montagna P, Gasser T, Lehmann-Horn F, Dichgans M. Variability of familial hemiplegic migraine with novel A1A2 Na+/K+-ATPase variants. Neurology. 2004 May 25;62(10):1857-61.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15159495
- Pietrobon D. Familial hemiplegic migraine. Neurotherapeutics. 2007 Apr;4(2):274-84. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17395138
- Riant F, De Fusco M, Aridon P, Ducros A, Ploton C, Marchelli F, Maciazek J, Bousser MG, Casari G, Tournier-Lasserve E. ATP1A2 mutations in 11 families with familial hemiplegic migraine. Hum Mutat. 2005 Sep;26(3):281.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16088919
- Riant F, Ducros A, Ploton C, Barbance C, Depienne C, Tournier-Lasserve E. De novo mutations in ATP1A2 and CACNA1A are frequent in early-onset sporadic hemiplegic migraine. Neurology. 2010 Sep 14;75(11):967-72. doi: 10.1212/WNL.0b013e3181f25e8f.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20837964
- Swoboda KJ, Kanavakis E, Xaidara A, Johnson JE, Leppert MF, Schlesinger-Massart MB, Ptacek LJ, Silver K, Youroukos S. Alternating hemiplegia of childhood or familial hemiplegic migraine? A novel ATP1A2 mutation. Ann Neurol. 2004 Jun;55(6):884-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15174025

- Tavraz NN, Dürr KL, Koenderink JB, Freilinger T, Bamberg E, Dichgans M, Friedrich T. Impaired plasma membrane targeting or protein stability by certain ATP1A2 mutations identified in sporadic or familial hemiplegic migraine. Channels (Austin). 2009 Mar-Apr;3(2):82-7. Epub 2009 Mar 3. *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/19372756
- de Vries B, Freilinger T, Vanmolkot KR, Koenderink JB, Stam AH, Terwindt GM, Babini E, van den Boogerd EH, van den Heuvel JJ, Frants RR, Haan J, Pusch M, van den Maagdenberg AM, Ferrari MD, Dichgans M. Systematic analysis of three FHM genes in 39 sporadic patients with hemiplegic migraine. Neurology. 2007 Dec 4;69(23):2170-6. *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/18056581

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